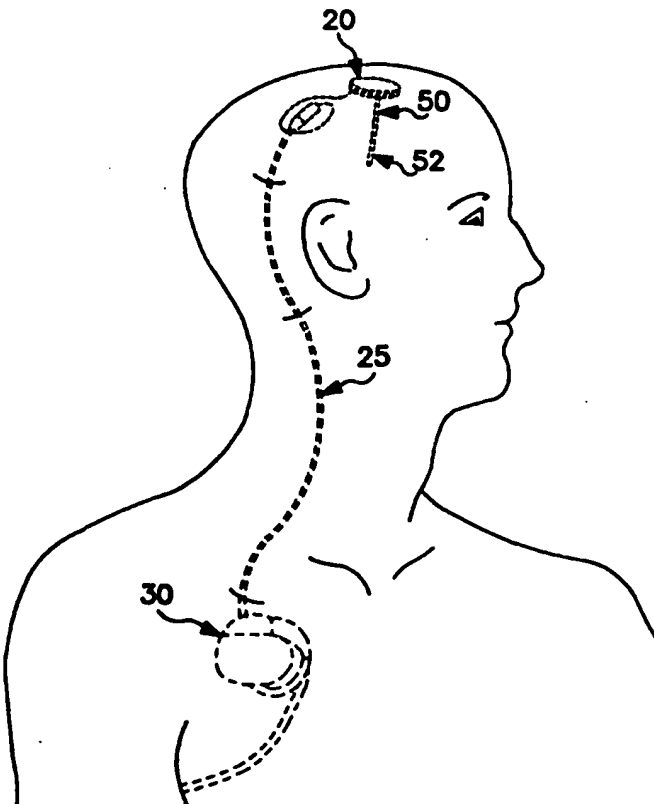


**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification <sup>6</sup>:</b> A61N 1/36	<b>A1</b>	<b>(11) International Publication Number:</b> WO 99/56821 <b>(43) International Publication Date:</b> 11 November 1999 (11.11.99)
<b>(21) International Application Number:</b> PCT/US99/07937 <b>(22) International Filing Date:</b> 12 April 1999 (12.04.99)  <b>(30) Priority Data:</b> 09/069,917      30 April 1998 (30.04.98)      US  <b>(71) Applicant:</b> MEDTRONIC, INC. [US/US]; 7000 Central Avenue N.E., Minneapolis, MN 55432 (US).  <b>(72) Inventor:</b> RISE, Mark, T.; 7745 Aetna Avenue N.E., Monticello, MN 55362 (US).  <b>(74) Agents:</b> KINGHORN, Curtis, D. et al.; Medtronic, Inc., 7000 Central Avenue N.E., MS301, Minneapolis, MN 55432 (US).		<b>(81) Designated States:</b> AU, CA, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).  <b>Published</b> <i>With international search report.</i>
<b>(54) Title:</b> IMPLANTABLE SEIZURE WARNING SYSTEM  <b>(57) Abstract</b> <p>The present invention discloses techniques for warning a patient of a possible onset of a seizure using a sensor, a signal generator and at least one implantable electrode. The electrodes are positioned to stimulate the spinal cord or under the skin. The sensor senses a parameter of the body indicative of the possible onset of a seizure. The sensor generates a sensing signal which is processed and an algorithm is utilized to determine whether the sensing signal shows a pattern indicative of a possible seizure onset. If such a pattern is recognized, the signal generator provides electrical stimulation via electrodes to generate a sensory stimulus to the body. The stimulation may provide visual, aural or touch stimulus to the patient. The patient is thereby alerted to the possibility of a seizure onset and may take appropriate action.</p> 		

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

## IMPLANTABLE SEIZURE WARNING SYSTEM

### Field of the Invention

This invention relates to the treatment of seizure disorders and, and more particularly relates to techniques for warning patients of an epileptic seizure.

### Description of Related Art

Epilepsy is a condition characterized by recurrent seizures which are the outward manifestation of excessive and/or hyper-synchronous abnormal electrical activity of neurons in the cerebral cortex of the brain. A seizure often occurs when the electrical activity of the brain becomes more "synchronized" as would be the case when the person is in a drowsy state.

A seizure patient may suffer from any combination of different types of seizures. Grand mal seizures are the most common form of epilepsy and are characterized by convulsions with tonic-clonic contractions of the muscles. Absence seizures (previously referred to as "petit mal") are characterized by a brief and sudden loss of consciousness. The psychomotor form of seizures is characterized by a clouding of consciousness for one or two minutes. A complex partial seizure is characterized by a complete loss of consciousness. The type of seizure experienced is typically dependent upon the function of the portion of the cerebral cortex where hypersynchronous activity is occurring. Many types of seizures generally involve the entire brain, while certain types, such as partial seizures, begin in one part of the brain and may remain local.

Regardless of the type of epilepsy, seizures significantly limit the autonomy of the patient. When hit with a seizure attack, the patient typically loses some level of control of his/her body. In most cases, seizures occur without prior warning to the patient. As a result, epileptic seizures pose a serious safety hazard to the patient as others surrounding the patient. For example, a patient hit with a sudden seizure attack while he/she is driving a car may endanger his/her own safety as well as the safety of others. Seizure patients are also exposed to a risk of bodily harm when operating machinery and even in daily activities such as crossing a street or going down stairs.

Researchers have developed a number of techniques for treating seizure disorders and its symptoms. For example, research has shown that inhibiting (namely,

reducing the excitation of neurons) the substantia nigra in the brain increases the threshold for seizure occurrence. Researchers have also found that increasing the activity of neurons in the external Globus Pallidum (GPe) increases inhibition of neurons in the subthalamic nucleus which in turn inhibits neural activity in the substantia nigra. Neurosurgeons have also been able to diminish the symptoms of many neural disorders by lesioning certain brain areas, examples being lesioning the ventral lateral portion of the internal Globus Pallidus and the Vim Thalamus for treating movement disorders. Alternatively, it has been demonstrated that open-loop Deep Brain Stimulation (DBS) at high frequencies (100 Hz or higher) of certain brain structures can alleviate, diminish, or completely stop symptoms of tremor, rigidity, akinesia or hemiballism much like creating a lesion. Electrical stimulation of the nervous system has also been used to suppress seizures. Finally, infusion of certain drugs into a region of the brain can affect the excitability of the neurons at the site of infusion as disclosed in U.S. Patent No. 5,713,923 (Rise et al.) assigned to Medtronic, Inc.

Others have studied the effects of electrically stimulating the vagus nerve as a means of "desynchronizing" the electrical activity of the brain. It has been observed that stimulation of the vagus nerve with certain parameters caused de-synchronization of the brain's electrical activity in animal models. These concepts were disclosed by Zabara in U.S. Patent Nos. 4,867,164 and 5,025,807. De-synchronization can be thought of as "alerting" phenomena since it reflects active mental activity.

Under another approach, researchers have devised algorithms to detect the onset of a seizure. Qu and Gotman reported a system that recognizes patterns of electrical activity similar to a template developed from recording an actual seizure. See H. Qu and J. Gotman, "A Seizure Warning System for Long-term Epilepsy Monitoring", *Neurology*, 1995;45:2250-2254. Similarly, Osario et. al. have reported an algorithm applied to signals recorded from intracranial electrodes capable of 100% seizure detection rate with 0% false negatives and minimal false positives. See I. Osario, M. Frei, D. Lerner, S. Wilkinson, "A Method for Accurate Automated Real-time Seizure Detection", *Epilepsia*, Vol. 36, Suppl. 4, 1995. In each of these techniques for recognizing the onset of a seizure, the developers employ two processes. The first

process is to extract certain features from the signals representing the electrical activity of the brain. Examples of the signal features include the signal power or the frequency spectrum of the signals. The second process is to recognize a pattern or set of values for those features which characterize a brain state that will reliably lead to a seizure.

5           Using these pattern recognition techniques, researchers have developed warning systems to alert the seizure patient of a possible seizure onset. For example, U.S. Patent Nos. 3,863,625 and 4,566,464 disclose epileptic seizure warning systems producing audio and visual warning signals to the patient prior to the possible onset of a seizure. The warning devices are external devices which can be worn in a shirt pocket of a  
10           seizure patient. Such an approach is generally simpler in design than the above-described techniques for treatment of seizures and provides the patient prior warning of a possible seizure onset. Advantageously over the above-mentioned methods, these device allows the patient to take appropriate action to minimize physical injury to the patient and others. This approach, however, requires the patient to constantly carry  
15           around the monitoring device causing inconvenience to the patient especially if the monitoring device is misplaced. The use of audio and visual signals as the warning mechanism may also not be as effective if the device is buried underneath a heavy coat or is outside of the hearing range of the patient. In addition, this device is ineffective for seizure patients who have impaired vision or hearing.

20           The present invention is directed to overcoming the disadvantages of the foregoing systems.

### **SUMMARY OF THE INVENTION**

As explained in more detail below, the present invention overcomes the above-noted and other shortcomings of prior techniques for warning of epileptic seizures.

25           A preferred form of the invention consists of a sensing portion capable of detecting the onset of a seizure, a signal processing portion, and a therapy delivery portion. The sensing portion may be an electrical sensor, chemical sensor, and/or a sensor for sensing physiological changes. The particular structure and parameter to measure may be selected from any known techniques which provide indication of the possible onset of a  
30           seizure. The signal processing portion processes and analyzes the sensed signal using an

algorithm for recognizing a pattern scheme indicative of the onset of a seizure. If a pattern indicative of the onset of a seizure is recognized, the therapy delivery portion is triggered. The therapy delivery portion is preferably a stimulation electrode which delivers sensory stimulation to the patient thereby alerting the patient of the onset of a seizure.

Sensory stimulation may encompass any combination of touch, sight or sound stimuli. The patient may then take appropriate action to avoid physical injury. For example, if the patient is driving a car when he/she is given a warning signal under the present invention, the patient may immediately stop the car. Further, research has found that the human body is capable of aborting seizures through sensory self stimulation. For example, some patients who have a sensory experience associated with a partial seizure, called an aura, will slap themselves to prevent the generalized seizure that normally follows. Accordingly, under the present invention, if a patient is provided sensory stimulation warning the patient of the possibility of a seizure onset, the patient may take similar action to prevent the seizure. In fact, if the sensory stimulation is sufficiently intense, it may obviate the need for the patient to do anything since the sensory stimulation is equivalent to slapping themselves. Moreover, the cognitive recognition of the possibility of a seizure may in itself serve to abort the occurrence of the seizure. For example, the patient may engage in a mental activity such as performing mathematical computations to "de-synchronize" the neurons, thereby reducing the hypersynchronous of the neurons.

Under another embodiment, the invention includes a sensing portion, a signal generating portion and a therapy delivery portion. Under this embodiment, the sensing portion monitors electrical, chemical and/or physiological activity of the patient. The signal generating portion transduces the sensed activity of the patient to a corresponding electrical signal. The therapy delivery portion provides sensory stimulation to the patient based on the electrical signal provided by the signal generating portion. Sensory stimulation may be provided by stimulation of the dorsal column of the spinal cord. Alternatively it may be provided by stimulation of a region of the thalamus or cortex representing a sensory function such as skin sensation or sound, visual or olfactory

perception. The patient is thereby provided continuous sensory stimulus relating to electrical, chemical and/or physiological activity of the patient sensed by the sensing portion. Before the patient experiences a seizure, the patient will have sensed a certain pattern of sensory stimulus. After one or more of such seizure episodes, the patient may thereby learn to recognize patterns which are indicative of a seizure onset. By recognizing these patterns, the patient may thereby take appropriate action as discussed herein.

By using the foregoing techniques, seizure disorders, including epilepsy, can be treated and seizures can be alleviated or prevented using sensory stimulation to consciously alert the patient of the onset of a seizure. By alerting the patient of a possible seizure onset, the patient may take action to minimize the risk of injury result from a loss of bodily control. Moreover, mental awareness by the patient of the possibility of a seizure in itself may thereby prevent the seizure from occurring. Examples of the more important features of this invention have been broadly outlined above in order that the detailed description that follows may be better understood and so that contributions which this invention provides to the art may be better appreciated. There are, of course, additional features of the invention which will be described herein and which will be included within the subject matter of the claims appended hereto.

#### **BRIEF DESCRIPTION OF THE DRAWINGS**

These and other advantages and features of the invention will become apparent upon reading the following detailed description and referring to the accompanying drawings in which like numbers refer to like parts throughout and in which:

Figure 1 is a diagrammatic illustration of a preferred embodiment of the present invention having a sensor implanted in a brain, a signal generator and stimulation electrodes;

Figure 2 is a diagrammatic illustration of the embodiment of Figure 1 depicting the placement of the stimulation electrodes to stimulate a predetermined site of the spinal cord;

Figure 3 is a block diagram of the signal processing portion of the present invention; and

Figure 4 is a flow chart depicting the steps for alerting the patient of a possible seizure.

### **DESCRIPTION OF THE PREFERRED EMBODIMENTS**

The present invention discloses techniques for providing sensory stimulation as a means for desynchronizing the electrical activity of the brain which leads to a seizure. As preferred, the invention includes generally a sensor portion for monitoring the onset of a seizure, a signal processing portion for processing the sensed signals to recognize a pattern indicative of a seizure onset, and a therapy delivery portion for providing sensory stimulation to alert the patient of the possible onset of a seizure.

Referring to Figures 1 and 2, a system made in accordance with the preferred embodiment may be implanted below the skin of a patient. The system includes generally a sensor 20, a signal processor/generator 30 and one or more stimulation electrodes 40.

Sensor 20 serves as the sensing portion of the present invention. Sensor 20 is implanted into a portion of a patient's body suitable for detecting a condition resulting from the onset of a seizure, including a seizure itself. Sensor 20 is adapted to sense an attribute of the body that changes in advance of or during a seizure. Sensor 20 is operatively coupled to provided sensed signals to the signal processor/generator 30. As shown, sensor is coupled via lead 25 to signal processor/generator 30. Alternatively, telemetry may be used to couple components 20 and 30. Signals that are received by the sensor may be amplified before transmission to signal processor/generator 30.

Sensor 20 may take the form of a device capable of detecting nerve cell or axon activity that is related to the pathways at the cause of a seizure symptom, or that indicates sensations which are elicited by the onset of a seizure. As preferred, sensor 20 is located deep in the brain parenchyma in appropriate locations as shown in Figure 1 and consists of a tube 50 implanted into brain B that carries one or more depth wire electrodes near end 52 of tube 50. For such detecting, the electrodes may be inserted into the thalamus, internal capsule, hippocampus, cortex or basal ganglia of brain B. Alternatively, the electrodes may be inserted into the seizure focus or part of the central nervous system where seizures begin.



In other embodiments, sensor 20 may include electrical transducers including subcutaneous electrodes placed on the surface of the skull over appropriate brain structures, peg electrodes implanted into the skull over these brain structures, epidural electrodes, or subdural electrodes placed on the cortical surface of appropriate brain structures. Under these embodiments, brain EEG/ECOG recorded above the cortical surface also may be detected by such a sensor. Sensors placed above the cortical surface may be generally located at two or more locations identified in the International 10-20 system of standard sites for EEG (*Spehlmann's EEG Primer, Second Edition*, Bruce J. Fisch, Elsevier Sciences Publisher BV, 1991).

Alternatively, sensor 20 may be a chemical sensor implanted in the brain B or ventricular space for detecting certain chemical substances such as transmitter substances or the break down products of transmitter substances. Under this alternative, sensor 20 may take the form of a transducer consisting of an electrode with an ion selective coating applied which is capable of directly transducing the amount of a particular transmitter substance or its breakdown by-products found in the interstitial space of a region of the brain B such as the hippocampus or thalamus. The level of the interstitial transmitter substance is an indicator of the relative activity of the brain region and the onset of a seizure. An example of this type of transducer is described in the paper "Multichannel semiconductor-based electrodes for in vivo electrochemical and electro-physiological studies in rat CNS" by Craig G. van Hone, Spencer Bement, Barry J. Hoffer, and Greg A. Gerhardt, published in *Neuroscience Letters*, 120 (1990) 249-252.

As yet another alternative, sensor 20 may sense physiological changes which are indicative of a seizure onset. For example, sensor 20 may transduce physiological changes in the heart rate or respiration. Under this alternative, sensor 20 may be placed near nerve cells controlling muscles and include a device capable of detecting nerve compound action potentials (e.g., either sensory afferent information from muscle or skin receptors or efferent motor potentials controlling a muscle of interest). Alternatively, sensor 20 may detect muscle EMG in one, two or more muscles. Monitored muscles may include the heart, respiratory muscles or reciprocal muscles at

one joint. For such detection, sensor 20 may take the form of a lead with one or more recording electrodes inserted into the muscle of interest. In yet other embodiments, sensor 20 may sense heart rate or respiration rate. Sensor 20 may be physically located outside of the body and communicate with the implanted portion through telemetry.

5           The output of sensor 20 is coupled by cable 25, comprising one or more conductors, to the signal processing portion of the present invention. Alternatively, the output of an external sensor would communicate with the implanted pulse generator through a telemetry downlink. Such telemetric systems may use, for example, radio frequency, ultrasound, infrared or other like communication means.

10           The signal processing portion of the present invention is preferably included within signal processor/generator 30. Alternatively, signal processor/generator 30 may be separated into a signal processing component and a signal generating component. The signal processing portion or component provides a means for signal processing and means for pattern recognition. Figure 3 is a block diagram depicting the signal  
15           processing portion of the present invention. A signal received from sensor 20 may be processed by amplifying and filtering the signal by amplifier 100 and filter 200 respectively. The signal is then converted to a digital representation by analog to digital converter 300. The signal may then be further processed by a digital signal processing chip 400 or may be input to a microprocessor 500. Microprocessor processes the sensor  
20           data in different ways depending on the type of parameter that is sensed by sensor 20. Microprocessor 500 processes the sensor signal and determines whether there exists a threat of a seizure. In particular, microprocessor 500 serves as the means for feature extraction and for pattern recognition. Alternatively, digital signal processing chip 400 could be used to extract features prior to processing by the software algorithm of  
25           microprocessor 500. Feature extraction and pattern recognition involves implementing an algorithm to detect the onset of a seizure.

          In a preferred embodiment, the software algorithm is performed as follows. Sixteen channels of EEG waves are recorded. These EEG waves are then low-pass filtered at 70 cycles/sec with a 4-pole analog filter and then sampled at 200  
30           samples/sec/channel. The resulting signal is then broken down into simple features by

reducing the sinusoidal EEG signal into a sequences of segments. A segment is a section between two consecutive extremes of amplitude and is characterized by duration, amplitude and direction (i.e., slope of the line). A sequence of segments is created to eliminate small amplitude "noise" (beta frequency EEG, muscle artifact).

5 This noise creates smaller intervening segments that face an opposite direction to that of the neighboring larger segments. The sequence combines one or more segments which are faced in the same direction and smaller intervening segments. A sequence ends when a segment not belonging to that sequence is produced. A segment does not belong to a sequence when its direction is opposite to the previous segment and its length is

10 greater than the length of the previous segment. When a sequence is complete, the following operations take place sequentially to determine whether a possible EEG spike or sharp wave (SSW) is detected. First, the relative amplitude of the current sequence and of the preceding one is checked to determine whether they are above a certain threshold. The relative amplitude is the amplitude of the sequence relative to the

15 average amplitudes of the sequences 5 seconds prior to the instant sequence. The relative amplitude is the ratio of the amplitude of the instant sequence to the average amplitude of the previous sequences taken 5 seconds prior. If the relative amplitude is above 4, then the sequence is marked as being part of a SSW. Next, the pseudo-duration of the segment is checked. The pseudo-duration is graphically determined by extending

20 a line from the start of a sequence (point A) through the half-way point of the actual EEG wave and extending it so its end (point B) equals the amplitude level of the ending point of the sequence. The horizontal distance from A to B is the pseudo-duration. The sequence is marked as a possible SSW if the pseudo-duration in combination with the relative amplitude reaches above a certain amount. Generally, the shorter the pseudo-

25 duration, the lower the relative amplitude needs to be for a SSW marking. Next, the relative amplitudes are checked in relation to the relative sharpness of the waves. The relative sharpness of the wave is the second derivative of a wave at 15 msec before and after the apex of a wave. The higher the relative sharpness, the lower the relative amplitude required to mark the sequence as a possible SSW. Finally, the total duration

of the wave is checked. If it is larger or equal to 35 msec, the sequence is marked as a possible SSW.

Once a sequence or a wave is marked as a possible SSW, further processing is required to possibly reject this wave. For example, the wave is rejected if it is the result of muscle activity, eye blinks or alpha activity. Muscle activity may cause a large number of high amplitude segments in the immediate surrounding of the wave (1/3 sec). Eye blinks may cause SSW marking from an EEG in the frontal channel having positive polarity, has a duration larger than 150 msec, and a wave of similar amplitude occurs simultaneously on the homologous contralateral channel. Alpha activity causes a dominant frequency of 8-12 cycles/sec.

Once a wave is determined to be a SSW, its relationships with other channels are important for localization of an epileptic focus. The above analysis proceeds by discrete time units of about 1/3 sec. If several SSWs are found in a given channel during a time unit, only the sharpest is retained. If SSWs are found in one or more channels within the time unit, an event is said to have occurred. The events from the 16 EEG channels may then be tabulated. Based on the location and occurrence frequency of these events, electrical activity indicating a seizure pattern may be determined. Such a system may be that disclosed by J. Gotman and P. Gloor in *Automatic Recognition and Quantification of Interictal Epileptic Activity in the Human Scalp EEG*, *Electroencephalography and Clinical Neurophysiology*, 41: 513-529, 1976. The rhythmicity of the electrical activity could also be used to indicate the occurrence of a seizure. The time interval associated with two successive segments is proportional to the frequency of EEG activity. Frequency of EEG activity between 3 to 20 cycles/sec sustained for a sufficient duration indicated the occurrence of a seizure. For example, once a patient suffers a seizure attack, a template may be created which can be used to detect future seizures exhibiting similar EEG activity. Such a template would be patient specific.

Other examples of algorithms to detect the onset of seizures have been reported in U.S. Patent Nos. 5,311,876 (issue May 17, 1994) and 5,349,962 (issued Sept. 27, 1994) and by Jean Gotman in *Epilepsy Surgery*, ch. 36 (ed. Hans, Luders, Raven Press, New York 1991) and Ivan Osorio & Mark Frei in *Abstracts of the American Epilepsy*

Society meeting, 1995. These references are incorporated herein by reference. Those skilled in the art will appreciate that any number of other algorithms may be used. An external electronic device may be implemented to telemeter parameter changes or newer algorithms to the implanted signal processing device to adapt the detection algorithm to the particular patient.

Microprocessor 500 is coupled to signal processor/generator 30 and cues the signal processor/generator 30 to generate a signal when a pattern indicative of a seizure is identified. Signal processor/generator 30 is implanted in a human body in a subclavicular, subcutaneous pocket. Alternatively, the signal processor/generator 30 may be implanted elsewhere, such as in the abdomen. Signal processor/generator 30 may take the form of a modified signal generator Model 7424 manufactured by Medtronic, Inc. under the trademark Itrel II which is incorporated by reference. Signal processor/generator 30 may include a frequency generator, a digital to analog converter, and a pulse width control module to vary the type of stimulation to provide as a warning. The stimulus pulse frequency is controlled by programming a value to the programmable frequency generator (not shown). The programmable frequency generator provides an interrupt signal to signal processor/generator 30 when each stimulus pulse is to be generated. The frequency generator may be implemented by model CDP1878 sold by Harris Corporation.

At the time the present invention is implanted within the patient, the clinician programs certain key parameters into the memory of the implanted device or may do so via telemetry. These parameters may be updated subsequently as needed. Alternatively, the clinician may elect to use default values. The clinician must program the range of values for pulse width, amplitude and frequency which microprocessor 500 may use to optimize the therapy. Stimulus parameters can be adjusted (via telemetry) by a computer algorithm within a range specified by the clinician in an attempt to optimize the seizure suppression.

Figure 4 discloses a flow chart for providing a patient with a seizure in accordance with the present invention. At step 405, sensor 20 senses a parameter of the body and generates a signal. At step 410, the signal is processed and, at 415, an

algorithm determines whether the sensed signal indicates that there exists a risk of a seizure onset. This step is continually performed. If it is determined that a seizure onset is possible, at step 420, electrodes 40 provide electrical stimulation to provide some sort of sensory stimulus to alert the patient. Alternatively, the sensory stimulus may be strong enough such that it in itself may abort the onset of a seizure.

Simulation electrodes 40 serve as the therapy delivery portion of the present invention. Each electrode 40 is individually connected to the signal processor/generator 30 through a wire conductor. Depending upon the stimulus desired, any number of electrodes may be used. Model 3387 DBS<sup>TM</sup> electrodes sold by Medtronic, Inc. of Minneapolis, Minnesota may be used. Stimulation electrodes 40 serve to produce a sensory experience for the patient based on the signal provided by the signal processor/generator 30. Under the embodiment of Figure 1, the stimulation electrodes 40 are placed along the spinal cord in the epidural space. The exact placement of the electrodes 40 is dependent upon the type of sensory experience desired. Sensors may be placed to automatically elicit a visual, aural or touch stimulus. An alternative sound stimulus may be an speaker mechanism as found in synchroed pumps. For example, Synchroed® model 8616 pump sold by Medtronic, Inc. may be used. Alternatively, sound may be generated via a piezoelectric sound generator. Alternatively, any combination of touch stimulus, sight stimulus and sound stimulus may be utilized.

In another application, a large sensory stimulus may be desired where the sensory stimulus in itself would serve to prevent the onset of a seizure. In such a case, electrodes 40 may be placed along the anterolateral aspect of the spinal cord to activate the pain fibers of the spinothalamic tract thereby creating a more painful experience. Alternative placement of electrodes 40 may include the dorsal column of the spinal cord, the antero lateral column of the spinal cord, skin nerves, the auditory cortex, the somatosensory cortex, nuclei of sensory thalamus, or the visual cortex.

Yet another arrangement is placement of the electrodes 40 over the somatosensory cortex either by using peg electrodes in the skull (to sense EEG) or epidural electrodes slipped under the skull through a burr hole to stimulate the cortex. Still another option is use of a steerable electrode to allow changes to the desired

sensory stimulus. Such an electrode is disclosed U.S. Patent Application Serial No. 08/637,361 filed April 25, 1996 and entitled "Techniques for Adjusting the Locus of Excitation of Neural Tissue in the Spinal Cord or Brain." As another embodiment, electrodes 40 may be placed directly under the skin to produce skin senses.

5 In accordance with another embodiment of the present invention, the system includes generally a sensing portion, a signal generating portion and a therapy delivery portion. Under this embodiment, the sensing portion monitors electrical, chemical and/or physiological activity of the patient. The signal generating portion transduces the sensed activity of the patient to a corresponding electrical signal used to activate a  
10 pattern of sensation in one part of the sensory nervous system. The signal generating portion includes generally a signal generator. Under this embodiment, means for pattern recognition, such as algorithms, would not be required. The sensed signal is processed and the therapy delivery portion provides continuous sensory stimulation to the patient representative of the sensed electrical, chemical and/or physiological activity.

15 Alternatively, the patient may receive sensory stimulus in intervals of short time periods. For example intervals of 1-10 seconds may be utilized. Rather than provide the patient with sensory stimulation only when a possible seizure onset is calculated, the patient is provided continuous stimulation. The sensory stimulation provided includes features which are in some way related to the features extracted from the EEG/ECOG containing  
20 the most power. The stimulus intensity which is determined by the pulse width and amplitude of the stimulus pulses might be related to the amplitude of the EEG/ECOG. Alternatively, stimulus amplitude might be related to a measure of complexity as described by K. Lehnertz and C.E. Elger ("Neuronal complexity loss in temporal lobe epilepsy: effects of carbamazepine on the dynamics of the epileptogenic focus.",  
25 *Electroencephalography and clinical Neurophysiology*, 103 (1997) 376-380. Over time and after one or more seizure episodes, the patient will learn to recognize the stimulation patterns which are indicative of a seizure onset. The human brain which has an inherent ability to recognize patterns may thereby learn to recognize the patterns for the occurrence of seizures.

By using the foregoing techniques for electrical stimulation, seizure patients may be provided adequate warning of a possible seizure onset to avoid the risk of physical injury. The patient may also take action to avoid the possible onset of the seizure.

Those skilled in that art will recognize that the preferred embodiments may be altered or amended without departing from the true spirit and scope of the invention, as defined in the accompanying claims.



## I CLAIM:

1. A method of warning a patient of a possible onset of a seizure using a sensor, a signal generator and at least one implantable electrode having a proximal end and a stimulation portion, the method comprising the steps of:

5 surgically implanting the sensor within a body of a patient;

coupling the sensor to the signal generator;

surgically implanting the electrode in the body, coupling the proximal end to the signal generator, and positioning the stimulation portion to be in communication with neural tissue within the body; and

10 sensing a parameter of the body with the sensor and generating a sensing signal;

processing the sensing signal by the signal generator to recognize a pattern indicative of the onset of a seizure; and

if the pattern is recognized, stimulating the neural tissue with the electrode to generate a sensory stimulus to the body.

15 2. The method of claim 1, wherein the step of surgically implanting the sensor includes the step of positioning the sensor to be in communication with a predetermined site in a brain.

3. The method of claim 2, wherein the step of positioning includes the step of selecting the predetermined site from the group consisting of the thalamus, internal capsule, hippocampus, cortex and basal ganglia.

20 4. The method of claim 1, wherein the step of sensing includes the step of sensing electrical activity of a brain.

5. The method of claim 1, wherein the step of sensing includes the step of sensing chemical activity of a brain.

25 6. The method of claim 1, wherein the step of surgically implanting includes the step of surgically implanting the signal generator.

7. The method of claim 6, wherein the step of surgically implanting the signal generator includes the step of placing the signal generator in a subclavicular, subcutaneous pocket of the body.

8. The method of claim 6, wherein the step of surgically implanting the signal generator includes the step of placing the signal generator in an abdomen of the body.

9. The method of claim 1, wherein the step of processing the sensing signal includes the step of performing an algorithmic operation.

10. The method of claim 9, further comprising the step of changing the algorithmic operation to a second algorithmic operation.

11. The method of claim 1, wherein the step of stimulating includes the providing a type of stimulus selected from the group consisting of touch stimulus, visual stimulus, and aural stimulus.

12. The method of claim 1, wherein the step of surgically implanting the electrode includes the step of positioning the electrode to be in communication with a predetermined part of a spinal cord of the body.

13. The method of claim 12, wherein the step of positioning includes the step of selecting the predetermined part from the group consisting of an epidural space, dorsal aspect, anterolateral aspect, and spinothalamic tract.

14. The method of claim 1, wherein the step of surgically implanting the electrode includes the step of positioning the electrode to be in communication with a somatosensory cortex of the brain.

15. The method of claim 1, wherein the step of surgically implanting the electrode includes the step of positioning the electrode to be in communication neural tissue underneath skin tissue of the body.

16. An apparatus for warning a patient of a possible onset of a seizure comprising:

an implantable sensor capable of generating a sensing signal;

a signal processor coupled to receive the sensing signal and having means for signal processing, means for pattern recognition, and a signal generator for generating a stimulation signal; and

at least one electrode having a proximal end and stimulation portion, the proximal end being coupled to receive the stimulation signal, the stimulation portion coupled to stimulate neural tissue.

5 17. The apparatus of claim 16, wherein the implantable sensor comprises at least one sensing electrode.

18. The apparatus of claim 17, wherein the sensing electrode is selected from the group consisting of a peg electrode, epidural electrode, subdural electrode, and a subcutaneous electrode.

10 19. The apparatus of claim 16, wherein the implantable sensor includes a transducer and a sensing electrode having an ion selective coating.

20. The apparatus of claim 16, wherein the implantable sensor has means for sensing physiological changes of a body.

21. The apparatus of claim 16, wherein the means for signal processor includes an analog to digital converter, an amplifier and a filter.

15 22. The apparatus of claim 16, wherein the means for signal processing includes a microprocessor.

23. The apparatus of claim 16, wherein the means for pattern recognition includes a microprocessor.

20 24. The apparatus of claim 16, wherein the signal processor is an external device further comprising means for telemetrically communicating with the sensor and the electrode.

25. The apparatus of claim 16, wherein the signal generator further comprises a frequency generator, a digital to analog converter, and a pulse width control module.

25 26. The apparatus of claim 16, wherein the electrode is a steerable electrode.

27. A method of warning a patient of a possible onset of a seizure using a sensor, a signal generator and at least one implantable electrode having a proximal end and a stimulation portion, the method comprising the steps of:

surgically implanting the sensor within a body of a patient;

30 sensing a parameter of the body and generating a sensing signal;

coupling the signal generator to receive the sensing signal and to generate a therapy signal based on the sensing signal;

surgically implanting the electrode in the body, coupling the proximal end to receive the therapy signal, and positioning the stimulation portion to be in communication with neural tissue within the body; and

periodically stimulating the neural tissue to generate a sensory stimulus based on the therapy signal.

28. A method of preventing the onset of a seizure using a sensor, a signal generator and at least one implantable electrode having a proximal end and a stimulation portion, the method comprising the steps of:

surgically implanting the sensor within a body of a patient;

coupling the sensor to the signal generator;

surgically implanting the electrode in the body, coupling the proximal end to the signal generator, and positioning the stimulation portion to be in communication with neural tissue within the body; and

sensing a parameter of the body with the sensor and generating a sensing signal;

processing the sensing signal by the signal generator to recognize a pattern indicative of the onset of a seizure; and

if the pattern is recognized, providing a sensory stimulus to the neural tissue with the electrode to responsively initiate desynchronization of neural activity.

29. The method of claim 28, wherein the step of providing sensory stimulus includes the step of stimulating a predetermined portion of the neural tissue, the predetermined portion being selected from the group consisting of a dorsal column of a spinal cord, an antero lateral column of the spinal cord, skin nerves, auditory cortex, somatosensory cortex, nuclei of sensory thalamus, and visual cortex.

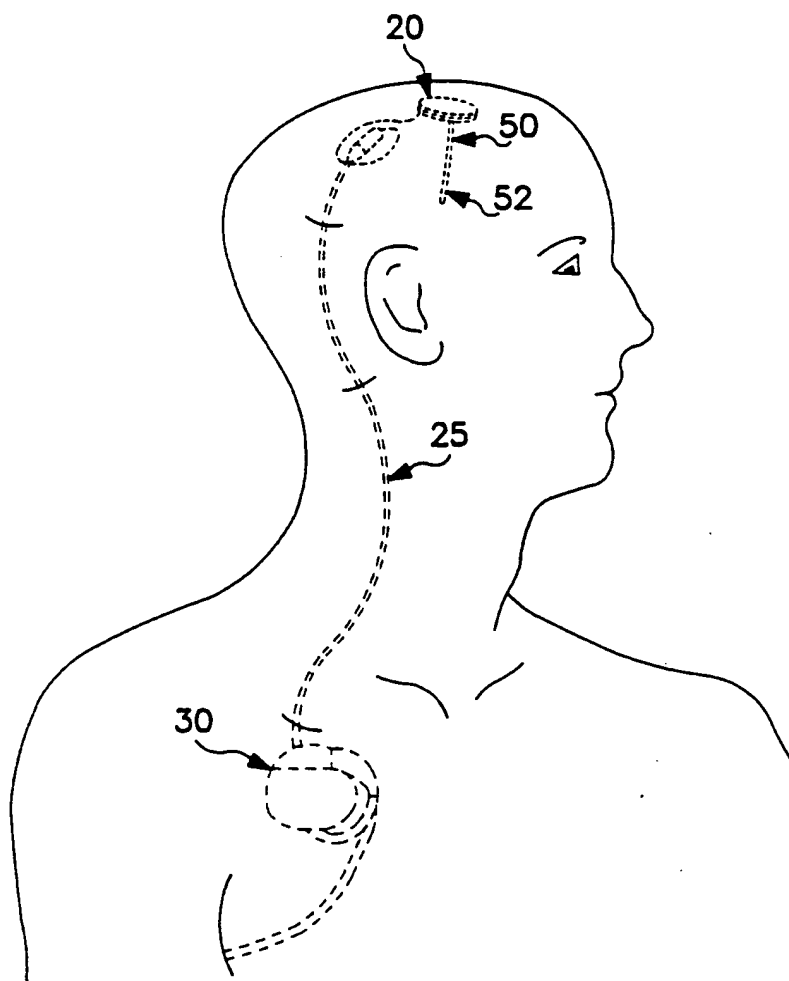


FIG. 1

2/4

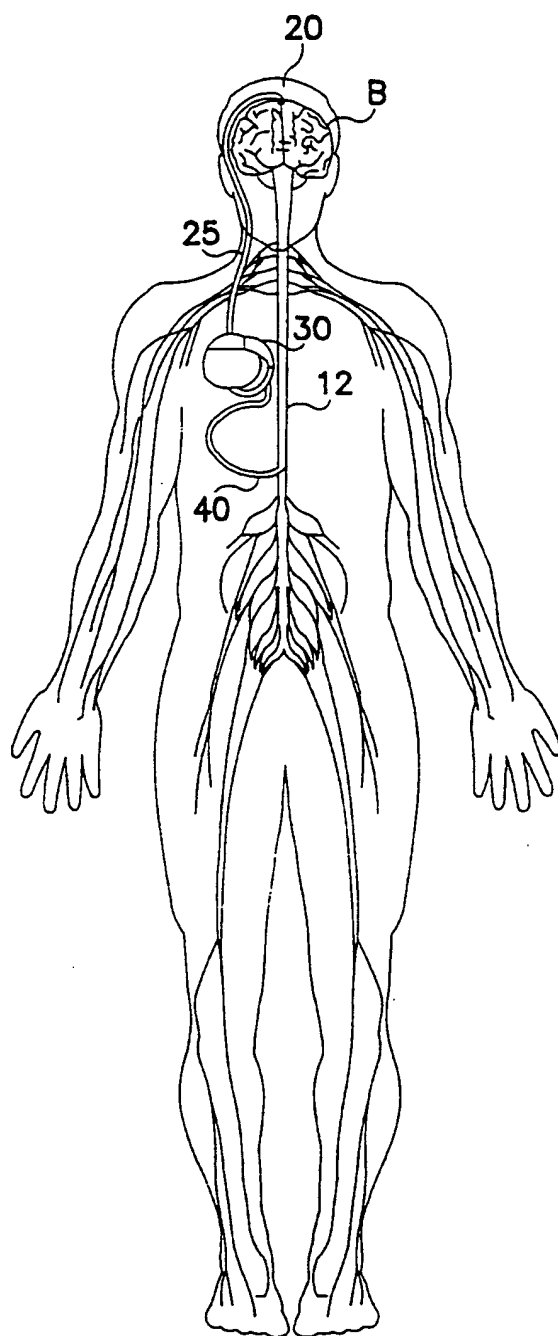


FIG. 2

3/4

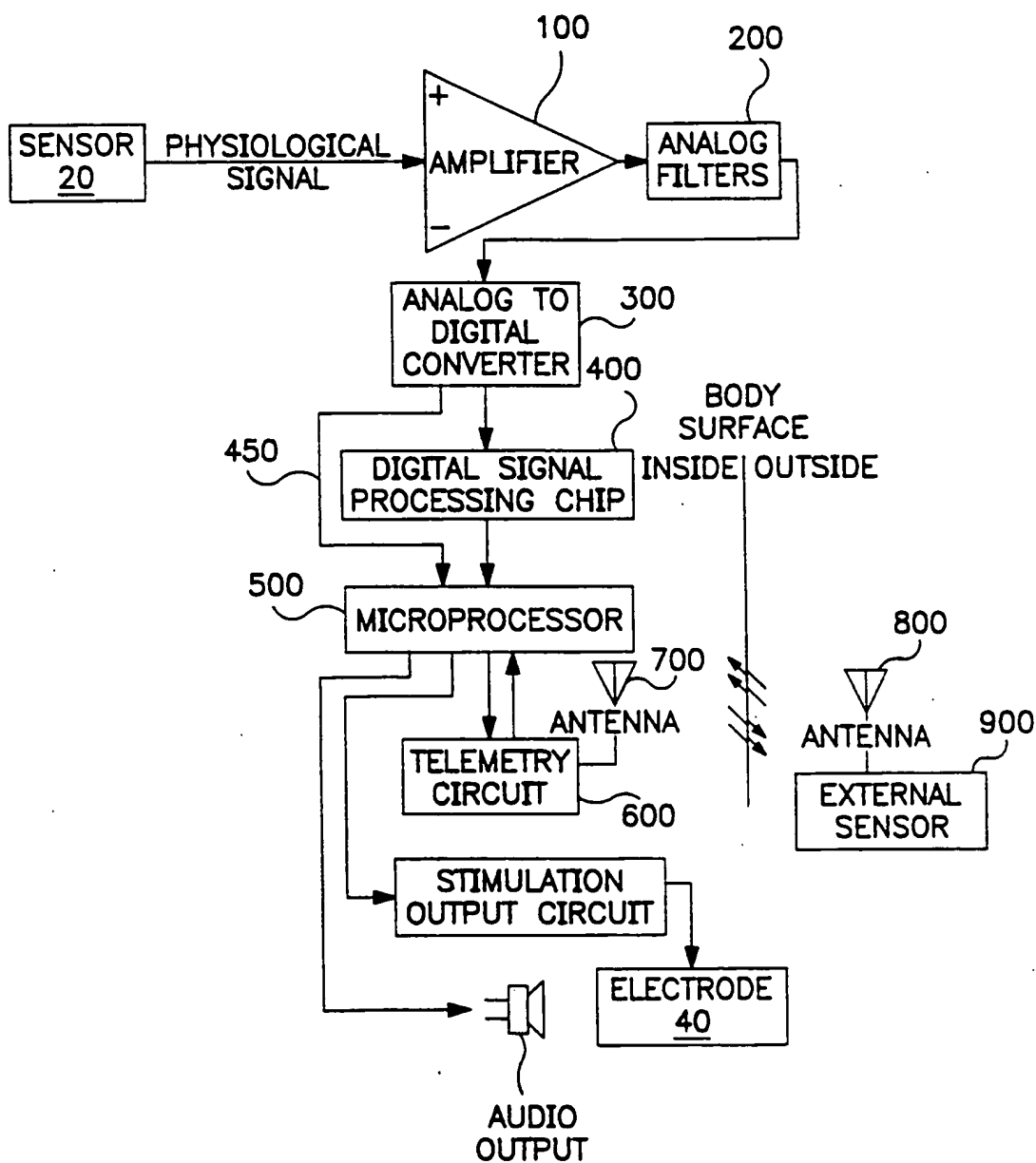


FIG. 3

4/4

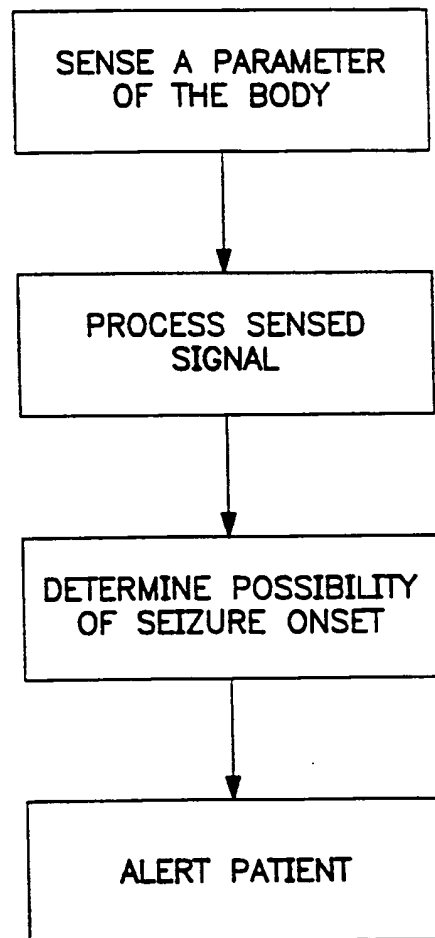


FIG. 4



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/07937

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A61N1/36

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 26823 A (UNIV KANSAS) 31 July 1997 (1997-07-31) page 4, line 20 - page 6, line 16 page 7, line 39 - page 9, line 11 page 15, line 4-8; figure 1	16-18, 20-25
A	---	26
X	US 5 713 923 A (RISE MARK T ET AL) 3 February 1998 (1998-02-03) cited in the application column 3, line 13 - column 6, line 7 column 8, line 29 - column 10, line 34; figures 1-6	16-25
X	US 5 683 422 A (RISE MARK T) 4 November 1997 (1997-11-04) the whole document	16-25
	---	
	---/---	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"S" document member of the same patent family

Date of the actual completion of the international search

27 July 1999

Date of mailing of the international search report

03/08/1999

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Allen, E

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/07937

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 566 464 A (PICCONE VINCENT A ET AL) 28 January 1986 (1986-01-28) the whole document ---	16-18, 22-24
A	US 3 863 625 A (VIGLIONE SAM S ET AL) 4 February 1975 (1975-02-04) abstract; figure 1 ---	16-18,24
E	EP 0 911 061 A (NEUROPACE INC) 28 April 1999 (1999-04-28) column 3, line 8 - column 4, line 41 column 7, line 45-56 column 9, line 18-47 column 13, line 39 - column 17, line 42 column 27, line 53-56 column 28, line 36-45 column 37, line 8 - column 39, line 18; figures -----	16-25

# INTERNATIONAL SEARCH REPORT

national application No.

PCT/US 99/07937

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-15, 27-29  
because they relate to subject matter not required to be searched by this Authority, namely:  
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/07937

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9726823 A	31-07-1997	AU 1752897 A EP 0898460 A	20-08-1997 03-03-1999
US 5713923 A	03-02-1998	AU 2746897 A EP 0904119 A WO 9742990 A	05-12-1997 31-03-1999 20-11-1997
US 5683422 A	04-11-1997	AU 2595397 A EP 0895483 A WO 9739795 A US 5792186 A	12-11-1997 10-02-1999 30-10-1997 11-08-1998
US 4566464 A	28-01-1986	NONE	
US 3863625 A	04-02-1975	NONE	
EP 0911061 A	28-04-1999	NONE	